PROPOSED RADIATION WEIGHTING FACTORS FOR USE IN CALCULATING PROBABILITY OF CAUSATION OF CANCERS

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This discussion considers approaches to establishing values of radiation weighting factors for different types of ionizing radiation for use in calculating the probability of causation of specific cancers in humans. Proposed probability distributions of radiation weighting factors in humans for different ionizing radiations of interest, taking uncertainties in the relevant radiobiological data into account, are presented. The ionizing radiations of concern to this discussion include photons (gamma rays and *X* rays), electrons, alpha particles, and neutrons. Except in the case of irradiation of the lung due to inhalation of radon and its short-lived decay products, the proposed probability distributions of radiation weighting factors in humans are intended to be applied in estimating the probability of causation of cancers in any organ or tissue and for any exposure situation.

Radiation weighting factors represent differences in the biological effectiveness of different radiations in causing stochastic effects in humans, primarily cancers. They take into account that, for a given absorbed dose in tissue, the probability of a stochastic response is assumed to depend on the radiation type, and sometimes its energy, as well as the absorbed dose. The values of radiation weighting factors are selected to represent data on the relative biological effectiveness (RBE) of the radiation type of concern, as obtained from relevant radiobiological studies. The RBE of radiation *i* compared with a reference radiation, *r*, is defined as the absorbed dose (D) of the reference radiation required to produce a specific level of response relative to the absorbed dose of the radiation type of concern required to produce an equal response:

$$\mathrm{RBE}_i = \frac{D_r}{D_i}, \tag{1}$$

with all physical and biological variables, except differences in radiation type, being held as constant as possible. Values of RBE are specific to each study, and they generally depend on the organism under study and the specific biological response of concern, the magnitude of the absorbed doses, the dose rate, and the dose per fraction if the dose is fractionated.

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In most determinations of RBE, the reference radiation is either orthovoltage *X* rays (usually in the energy range of 180-250 kVp) or higher-energy gamma rays produced in the decay of ^{60}Co or, less frequently, ^{137}Cs. Knowledge of the reference radiation in any study is important because, as discussed later, the biological effectiveness of *X* rays and gamma rays apparently is not the same and *X* rays generally are somewhat more effective in inducing stochastic responses. In this discussion, the reference radiation is taken to be high-energy gamma rays. This choice is appropriate for purposes of developing radiation weighting factors for use in estimating the probability of causation of cancers in humans because, except for exposures to radon, radiation risks in humans are estimated based primarily on data obtained from studies in the Japanese atomic-bomb survivors who were exposed mainly to higher-energy gamma rays.

Radiation Weighting Factors for Neutrons

RBEs for neutrons of various energies have been estimated in many studies involving different organisms, doses and dose rates, and stochastic responses (NCRP, 1990; NRPB, 1997). The doses and dose rates of neutrons and the reference radiations in these studies usually were substantially above levels of concern in estimating the probability of causation of cancers in radiation workers or members of the public. Therefore, there is a need to establish radiation weighting factors for neutrons that are appropriate at lower doses and dose rates.

The conventional approach to estimating cancer risks from exposure to neutrons at low doses and dose rates is based on estimates of RBEs at low doses and dose rates. These RBEs are obtained by extrapolation of data on dose-response for neutrons and the reference radiations at higher doses and dose rates. An RBE at low doses and dose rates obtained by this extrapolation procedure is commonly denoted by RBE_M. From an evaluation of values of RBE_M obtained from different studies that are deemed relevant to estimating cancer risks in humans, a representative radiation weighting factor at low doses and dose rates, denoted here by $w_{R,L}$, is chosen. Then, the cancer risk, *R*, from exposure to neutrons (*n*) at low doses and dose rates can be estimated as

$$R_n = w_{R,L} \times \frac{R_{\gamma,H}}{DDREF_\gamma}, \qquad (2)$$

where $R_{\gamma,H}$ is the cancer risk from exposure to gamma rays at high doses and high dose rates (e.g., the excess relative risk, ERR, per Sv, as determined from studies in the Japanese atomic-bomb survivors) and $DDREF_\gamma$ is the dose and dose-rate effectiveness factor for gamma rays in humans, which takes into account that cancer risks from exposure at low doses and dose rates of gamma rays (and other low-LET radiations) may be less than estimated risks at high doses and high dose rates in study populations. For example, for purposes of radiation protection, $DDREF_\gamma$ often is assumed to be 2; i.e., estimated cancer risks in the atomic-bomb survivors are reduced by a factor of 2 in estimating risks from exposure to gamma rays and other low-LET radiations at lower doses and dose rates (ICRP, 1991; NCRP, 1993).

When values of RBE_M for neutrons are estimated by extrapolation of dose-response data for neutrons and the reference radiations, the results obtained from different studies are found to vary widely. For example, reviews by the NCRP (1990) and NRPB (1997) indicate that best estimates of RBE_M for fission neutrons, as obtained from a variety of studies in small mammals, mammalian cell systems, and human lymphocytes in culture, vary from about 3 to perhaps 100 or more. Therefore, there is considerable uncertainty in the value of $w_{R,L}$ that should be used to represent these data for the purpose of estimating cancer risks in humans.

In studies used to estimate values of RBE_M, the dose-response relationships for neutrons usually appear to be linear at the lowest delivered doses. Therefore, the variability in the values of RBE_M obtained from the different studies, as noted above, probably is due mainly to pronounced differences in the linear-quadratic dose-response relationships for the low-LET reference radiations, which result in a wide range of DDREFs for these radiations (CIRRPC, 1995; NRPB, 1997; Edwards, 1999). That is, RBE_M is sensitive to changes in the biological effectiveness at low doses of the reference radiations, with higher values of RBE_M associated with high DDREFs for the reference radiations and lower values with low DDREFs. In effect, when risks at low doses and dose rates of neutrons are estimated using eq. (2), the DDREFs for the reference radiations (*X* rays or gamma rays) embodied in the values of RBE_M generally are not the same as the value of $DDREF_\gamma$ that might be used to adjust estimated cancer risks in humans exposed to gamma rays at high doses and high dose rates. Thus, the value of $w_{R,L}$ that might be chosen based on the estimates of RBE_M may not provide a reasonable representation of the biological effectiveness of low doses of neutrons in humans relative to low doses of gamma rays.

For the purpose of estimating the probability of causation of cancers in humans at low doses and dose rates of neutrons, the difficulties with obtaining a representative value of $w_{R,L}$ based on estimates of RBE_M can be addressed by using an alternative approach (CIRRPC, 1995; NRPB, 1997; Edwards, 1999). This approach is based on an assumption that the RBEs for neutrons used to estimate cancer risks in humans should be consistent with the data used to estimate cancer risks from exposure to photons. That is, the appropriate RBEs for neutrons are values that are obtained in studies using high acute doses of the low-LET reference radiations, because this was the condition of exposure of the atomic-bomb survivors from which most estimates of cancer risks in humans are obtained. Thus, if the DDREF for neutrons is assumed to be unity, based on the observation that the dose-response relationship usually is linear at the lower end of the range of delivered doses and the usual presumption of linearity at low doses and dose rates for all high-LET radiations, the risk from exposure to neutrons <u>at low doses and dose rates</u> can be estimated as

$$R_n = w_{R,H} \times R_{\gamma,H} , \qquad (3)$$

where $w_{R,H}$ is the radiation weighting factor that represents RBEs for neutrons at <u>high acute doses of the reference radiation</u> and $R_{\gamma,H}$ again is the risk from exposure to gamma rays <u>at high doses</u>

and high dose rates in the atomic-bomb survivors. Since the DDREF for neutrons is assumed to be unity, eq. (3) also applies at high doses and high dose rates of neutrons.

Using the alternative approach in eq. (3), there still is considerable variability in the RBEs for neutrons obtained from different studies at high acute doses of the reference radiations, due to the variety of biological systems and stochastic endpoints studied and the dependence of RBE on the dose of the reference radiation when its dose-response relationship is non-linear over the range of delivered doses, as is usually the case. However, this variability is considerably less than the variability in RBE_M when the conventional approach based on extrapolations of dose-response relationships for neutrons and the reference radiations described previously is used. Therefore, the uncertainty in the representative value of $w_{R,H}$ should be less than the uncertainty in the representative value of $w_{R,L}$ obtained using the conventional approach.

It should be emphasized that cancer risks at low doses and dose rates of neutrons estimated using either eq. (2) or eq. (3) would be the same if the DDREFs for the reference radiations in the determinations of RBE_M for neutrons were the same as the value of $DDREF_\gamma$ that is applied to the estimated risks at high doses and high dose rates of gamma rays in the Japanese atomic-bomb survivors. The advantage of the approach using eq. (3) is that it is compatible with the data in the atomic-bomb survivors on which most risk estimates are based and, thus, should provide more appropriate estimates of risk from exposure to neutrons at low doses and dose rates for purposes of estimating the probability of causation of cancers in humans.

Based on the foregoing considerations, we recommend that cancer risks from exposure to neutrons at any dose and dose rate be estimated using eq. (3). For fission neutrons, RBEs at high acute doses of the reference radiations can be obtained from an analysis by Edwards (1999); see also NRPB (1997). These RBEs are denoted by RBE_a by Edwards, but we use the notation RBE_H (CIRRPC, 1995). Based on data from several studies of life-shortening in mice, which is due mainly to induction of cancers, and induction of specific cancers in mice, Edwards derived a mean and standard deviation of RBE_H for each study. In some cases, two values of RBE_H and their uncertainties are given when the data are consistent with more than one interpretation. In all determinations of RBE_H except one, the reference radiation was higher-energy gamma rays. The one study in which *X* rays were the reference radiation is not included in the following discussion.

Values of RBE_H for fission neutrons obtained by Edwards (1999) from separate analyses of nearly 30 data sets range from less than 2 to about 20, taking the uncertainty in each estimate into account; the average of all estimates is about 6. Based on the distribution of the individual estimates of RBE_H, which appears to be lognormal, and the uncertainty in each estimate, we propose that the radiation weighting factor, $w_{R,H}$, for fission neutrons to be used in estimating cancer risks at any dose and dose rate in accordance with eq. (3) be described by a lognormal probability distribution having an arithmetic mean of 6 and an upper 97.5% confidence limit of 20. The 95% confidence interval of the proposed distribution lies between 1.2 and 20. Truncation of the lower tail of the distribution at 1.0, based on an assumption that the biological

effectiveness of neutrons would not be less than that of high-energy gamma rays, is discussed later in this section. The assumed probability distribution of $w_{R,H}$ applies to the spectrum of fission neutrons. In this spectrum, the energies range from 0.1-15 MeV, the most probable energy is 0.8 MeV, and the average energy is 2.0 MeV (Shleien et al., 1998).

In the proposed probability distribution of $w_{R,H}$ for fission neutrons, more than 60% of the values are less than the arithmetic mean of 6. This bias toward values less than the arithmetic mean can be justified by the following argument. In studies in small mammals that were used to estimate RBEs, a substantial fraction of the dose to target tissues was delivered by high-LET radiations (e.g., recoil protons). In humans, however, more of the dose to deep-lying organs and tissues would be delivered by low-LET gamma rays produced following absorption of thermalized neutrons by hydrogen nuclei. Therefore, RBEs obtained from studies in small mammals should tend to overestimate the biological effectiveness of incident fission neutrons in most organs and tissues of humans (ICRP, 1997; NRPB, 1997; Edwards, 1999). The proposed probability distribution of $w_{R,H}$ for fission neutrons is intended to take this into account.

The proposed probability distribution of $w_{R,H}$ for fission neutrons described above can be compared with the single-valued radiation weighting factors used by the U.S. Department of Energy (DOE) or recommended by the ICRP for purposes of radiation protection (i.e., in estimating equivalent doses and assessing compliance with dose limits). When there is insufficient information on the energy spectrum of neutrons, DOE regulations (10 CFR Part 835) specify a quality factor of 10 for all energies greater than 10 keV; this quality factor is essentially the same as $w_{R,L}$ in eq. (2). The ICRP's current recommendation on a radiation weighting factor that would apply to fission neutrons is 20 (ICRP, 1991), or twice the value used by DOE. The ICRP's value is based on estimates of RBE_M and, thus, would also be used to estimate cancer risks in humans in accordance with eq. (2). Now, if we assume a nominal $DDREF_\gamma$ of 2 (ICRP, 1991), the proposed probability distribution of $w_{R,H}$ described above would correspond to a distribution of $w_{R,L}$ having an arithmetic mean of 12 and a 95% confidence interval between 2.4 and 40.[2] Therefore, the proposed probability distribution of $w_{R,H}$ for fission neutrons is broadly compatible with the radiation weighting factors, $w_{R,L}$, at low doses and dose rates currently used by DOE and the ICRP; this probability distribution does not represent a reduction in estimated risks compared with risks that would be estimating using the DOE or ICRP radiation weighting factors.

A complication in estimating cancer risks from exposure to neutrons is the pronounced energy dependence of RBEs (NCRP, 1990; NRPB, 1997). DOE's representation of this energy

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[2]This confidence interval does not represent the range of values of $w_{R,L}$ for fission neutrons that would be obtained from analyses of different experiments, because $DDREF_\gamma$ for the reference radiation in the experiments may be substantially different from the nominal value of 2 assumed here. Values of $w_{R,L}$ for fission neutrons considerably greater than 40 can be obtained from some experiments (NCRP, 1990; Edwards, 1999).

dependence is the table of quality factors as a function of neutron energy in 10 CFR Part 835. The ICRP (1991) has taken a simpler approach in which the recommended radiation weighting factor is 5 for energies less than 10 keV, 10 for energies between 10 and 100 keV, 20 for energies between 100 keV and 2 MeV, 10 for energies between 2 and 20 MeV, and 5 for energies greater than 20 MeV. Thus, the proposed probability distribution of $w_{R,H}$ for fission neutrons that would be used to estimate cancer risks in accordance with eq. (3) applies to energies that are assumed by the ICRP to have the highest biological effectiveness. The reductions in the radiation weighting factor at lower and higher neutron energies recommended by the ICRP (1991) are based on limited data from studies in animals and cell cultures (NCRP, 1990; NRPB, 1997; Edwards, 1999) and considerations of the energy-dependence of the neutron quality factor (ICRU, 1986).

The ICRP (1991) also suggested that its recommended step function for $w_{R,L}$ described above can be represented by a smooth function of the form

$$w_{R,L} = 5 + 17\exp[-(\ln(2E))^2/6] \ , \qquad (4)$$

where E is the neutron energy in MeV. This relationship is not intended to imply any biological significance, but it does provide a convenient calculational tool when incident neutron energies are well known.

We propose that the energy dependence of the radiation weighting factor for neutrons, $w_{R,H}$, to be used in eq. (3) be defined in the following way. In the ICRP's step-function representation of $w_{R,L}$ described above, the values for energies other than 0.1-2 MeV are a factor of 2 or 4 less than the value that applies to fission neutrons. Thus, as a first approximation, when neutron energies are outside the range of 0.1-2 MeV, the proposed probability distribution of $w_{R,H}$ for fission neutrons described above could be reduced by a factor of 2 or 4, depending on the energy. For example, for 14-MeV neutrons produced by the ^{3}H(d,n)^{4}He reaction at low projectile energies, the result would be a lognormal probability distribution of $w_{R,H}$ having an arithmetic mean of 3 and an upper 97.5% confidence limit of 10; and for thermal neutrons, the probability distribution would have an arithmetic mean of 1.5 and an upper 97.5% confidence limit of 5.

However, the probability distributions of $w_{R,H}$ for neutron energies other than 0.1-2 MeV also should take into account that there is uncertainty in the assumed reduction in biological effectiveness by a factor of 2 or 4 compared with fission neutrons. Based on data discussed by Edwards (1999) and the NCRP (1990), we propose that the reduction factor of 2 for neutron energies of 10-100 keV or 2-20 MeV be represented by a triangular probability distribution having a lower bound of 1.5, a mode of 2, and an upper bound of 3, and that the reduction factor of 4 for neutron energies of <10 keV or >20 MeV be represented by a triangular probability distribution having a lower bound of 3, a mode of 4, and an upper bound of 6. Uncertainties in these reduction factors should be smaller than the assumed uncertainty in $w_{R,H}$ for fission neutrons.

An additional factor that should be considered in estimating cancer risks using eq. (3) is the possibility that the biological effectiveness of neutrons, and other high-LET radiations, increases as the dose rate decreases. This phenomenon is referred to as the inverse dose-rate effect. As discussed by the NCRP (1990), ICRP (1991), and CIRRPC (1995), some studies in mammals and mammalian cells at relatively high doses have shown an enhancement in the biological effectiveness of neutrons by up to a factor of about 2 when the same dose is delivered at lower dose rates. However, this effect is not seen in all studies at high cumulative doses, and it usually is not seen in studies at lower doses. Although it is not clear whether the mechanisms responsible for the observed inverse dose-rate effect for neutrons in some studies would apply in estimating cancer risks in humans, especially at low doses (CIRRPC, 1995), we propose that an additional correction be applied to eq. (3) to account for this effect. With this correction, the risk from exposure to neutrons would be estimated as

$$R_n = w_{R,H} \times EF \times R_{\gamma,H} , \quad (5)$$

where EF is an enhancement factor that represents the inverse dose-rate effect. This correction should be applied only in cases of chronic exposure to neutrons, but not to acute exposures.

Based on a review and summary of the limited data (CIRRPC, 1995) and taking into account the possibility that this effect does not apply in estimating cancer risks in humans, we propose a probability distribution for the enhancement factor for neutrons under conditions of chronic exposure that ranges from 1 to 2 and is weighted toward lower values – i.e., a discrete distribution with 50% of the values at 1, 25% at 1.5, and 25% at 2.

In summary, we propose that cancer risks in humans at any dose and dose rate of neutrons be estimated using an approach represented by eq. (3). The assumed biological effectiveness of neutrons in humans relative to high doses and high dose rates of gamma rays would be represented by a combination (aggregate) of two or three probability distributions that take into account the different factors of concern and their uncertainties. The first factor is the radiation weighting factor for fission neutrons; this factor would be used in estimating cancer risks for any exposure situation. The second factor, which would be used only when the incident neutron energies are outside the range of 0.1-2 MeV, is an energy-dependent reduction in biological effectiveness compared with fission neutrons. The third factor, which would be applied only in cases of chronic exposure, represents the inverse dose-rate effect.

Given the assumed probability distributions for each of the factors summarized above, the aggregate probability distributions representing the biological effectiveness of neutrons in specific cases will include some values less than 1.0. In all cases, however, the lower tail of the aggregate probability distribution should be truncated at 1.0. This truncation is based on an assumption that, since some of the dose due to incident neutrons of any energy would be delivered by high-LET radiations (NCRP 1971), the biological effectiveness of neutrons would not be less than that of high-energy gamma rays. The truncation of the lower tail at 1.0 should be applied only after the aggregate probability distribution representing the combination of all

relevant factors contributing to the biological effectiveness of neutrons for a given exposure situation is obtained.

Radiation Weighting Factors for Photons

For purposes of radiation protection, the radiation weighting factor for photons of any energy generally is assumed to be unity (ICRP, 1991; NCRP, 1993). However, data on the biological effectiveness of *X* rays (NCRP, 1990) and calculations of the energy-dependence of the photon quality factor (ICRU, 1986) indicate that photons of energy less than about 200 keV have a substantially greater biological effectiveness than higher-energy photons. Although an assumption that the biological effectiveness of photons is independent of energy may be satisfactory for purposes of radiation protection, we believe that estimates of the probability of causation of cancers in humans should take the apparently greater biological effectiveness of lower-energy photons into account. These considerations apply to *X* rays and any other photons of energy less than about 200 keV, such as the 60-keV gamma ray emitted in the decay of ^{241}Am.

Data on the biological effectiveness of 220-250 kVp *X* rays relative to high-energy gamma rays were reviewed by the NCRP (1990), and estimates of the relative biological effectiveness at low doses and dose rates, RBE_M, and their uncertainties were obtained. Since all estimates were obtained from studies of the same biological endpoint in the same biological system and essentially the same doses and dose rates of *X* rays and gamma rays were used in each study, we believe that the radiation weighting factor for *X* rays at low doses and dose rates, $w_{R,L}$, can be defined based on a weighted average of the values of RBE_M estimated by the NCRP, with each value weighted in inverse proportion to its uncertainty and the weighted values averaged in accordance with a root-mean-square calculation. Using this procedure, we obtain an estimated $w_{R,L}$ of 2.6 ± 0.5, where the uncertainty is the standard deviation. Based on this result, we propose that $w_{R,L}$ for photons of energy less than about 200 keV be described by a lognormal probability distribution having the 16th percentile at 2.1 and 84th percentile at 3.1. The 95% confidence interval of this distribution lies between 1.9 and 3.7, and the arithmetic mean is 2.6.

The radiation weighting factor described above is based on studies in which the average energy of the *X* rays was about 50-65 keV (Stanton et al., 1979; NCRP, 1985). Based on a calculation by the ICRU (1986) which indicates that the photon quality factor is essentially independent of energy in the range of about 30-200 keV, we believe that the result for *X* rays can be applied at any photon energy in this range. Thus, we propose that the probability distribution of $w_{R,L}$ described above be used to estimate cancer risks from exposure at low doses and dose rates of *X* rays and other photons of energy less than about 200 keV using eq. (2). The biological effectiveness of photons of energy less than 30 keV is considered below.

The calculation of the energy-dependence of the photon quality factor by the ICRU (1986) indicates that as the energy decreases below 30 keV, the biological effectiveness increases above the value at energies of 30-200 keV, and that the increase is greater than 50% as the energy

approaches 10 keV. For example, using the ICRU calculation, Brenner and Amols (1989) estimated that 23 kVp *X* rays should be about 1.3 times more effective than 44-250 kVp *X* rays in inducing breast cancer. Based on these results, we recommend that the proposed probability distribution of $w_{R,L}$ for photons of energy less than 200 keV be increased when the energy is less than 30 keV, and that the factor by which $w_{R,L}$ is increased be described by a triangular probability distribution having a lower bound of 1.0, a mode of 1.3, and an upper bound of 1.6.

As in the case of neutrons discussed previously, consideration needs to be given to whether the proposed radiation weighting factor at low doses and dose rates of lower-energy photons is suitable for use with estimated cancer risks in humans at high doses and high dose rates of high-energy gamma rays. The problem is more complicated than in the case of neutrons because the *X* rays and reference gamma radiations used in the studies both show linear-quadratic dose-response relationships. Furthermore, the dose-response relationships for *X* rays and gamma rays show distinctly different DDREFs, with the values for *X* rays being considerably lower than those for gamma rays. However, if we arbitrarily assume that the responses at 1 Gy obtained using the dose-response relationships for *X* rays and gamma rays (NCRP, 1990) can be used to approximate a best linear fit to the data over the range of delivered doses, we find that the average RBE for *X* rays at high doses and high dose rates would be about 1.4. If this value were used to estimate cancer risks from exposure to *X* rays at low doses and dose rates in accordance with eq. (3), the risks would be about the same as those obtained using eq. (2) and the central value of $w_{R,L}$ of 2.6 given above when a nominal $DDREF_\gamma$ of 2 (ICRP, 1991) is assumed. We believe that this comparison provides some indication that the use of eq. (2) with a lognormal probability distribution defined by a $w_{R,L}$ of 2.6 ± 0.5 is reasonable in estimating cancer risks from exposure to lower-energy photons at low doses and dose rates.

In estimating cancer risks in humans, acute exposure could be of concern for photons of any energy. In all such cases, cancer risks also would be estimated using eq. (2), and the biological effectiveness of photons of energy less than about 200 keV relative to high doses and high dose rates of high-energy gamma rays would be estimated using the factors described above. However, for acute doses of photons, the dose and dose-rate effectiveness factor ($DDREF_\gamma$) would be different (and generally lower) than in cases of chronic exposure. The probability distribution of $DDREF_\gamma$ for acute exposure depends on the magnitude of the dose, and a single value of 1.0 is assumed at doses above some value (see footnote a in Table 1).

Radiation Weighting Factor for Alpha Particles

Like neutrons, alpha particles are high-LET radiations that have been shown to be considerably more effective than low-LET radiations in inducing stochastic effects. Alpha particles also are presumed to have a linear dose-response relationship at any doses and dose rates below those where significant cell killing occurs. However, alpha particles are somewhat simpler than neutrons in that only a limited range of energies occurs in radioactive decay and any energy dependence of the biological effectiveness of alpha particles over this energy range

probably can be ignored. For purposes of radiation protection, the ICRP (1991) and NCRP (1993) recommend a radiation weighting factor of 20 for alpha particles of any energy.

Data on RBEs for alpha particles emitted in the decay of radionuclides have been reviewed by the NCRP (1990) and NRPB (1993); see also Sinclair (1996). Compared with neutrons, the estimation of RBEs for alpha particles is complicated by the fact that the reference radiation in most studies was not high-energy gamma rays. In some studies in mammalian cell systems, the reference radiation was *X* rays, and in studies of induction of bone or lung tumors in mammals, the reference radiation usually was the continuous spectrum of electrons (beta radiations) emitted in the decay of ^{90}Sr and its shorter-lived decay product ^{90}Y. However, the difference between using electrons from beta decay and high-energy gamma rays as the reference radiation may not be significant, because studies have indicated that exposures to electrons from ^{144}Ce decay and protracted exposures to ^{60}Co gamma rays are equally effective in producing chromosome aberrations in the liver of hamsters (NCRP, 1990).

Interpretation of data comparing induction of bone tumors in mammals by alpha-emitting radionuclides relative to ^{90}Sr/^{90}Y is further complicated by differences in the distributions of the study and reference radionuclides in cortical and trabecular bone compared with bone surfaces. These differences are important because the radiosensitive tissues in bone are located near the surface. For example, ^{239}Pu appears to be approximately 15 times more effective in inducing bone tumors in mice and dogs than ^{226}Ra when toxicity is estimated based on the average skeletal dose (NCRP, 1990), but this difference is due mainly to the fact that radium deposited in the skeleton becomes distributed throughout the volume of bone, as does strontium, but plutonium remains near the sites of deposition on bone surfaces. Similar effects are shown in studies of the toxicity of other alpha-emitting radionuclides, e.g., ^{241}Am and ^{243,244}Cm (NCRP, 1990).

Based on a review of animal studies, the NCRP (1990) concluded that the biological effectiveness of alpha particles relative to beta radiations in inducing bone and lung tumors and chromosome aberrations in the liver is in the range of about 15-50. However, values toward the upper end of this range were obtained from preliminary analyses, and a subsequent analysis of these data indicated a value less than 40 (Hahn et al., 1991). In addition, the value in one study reviewed by the NCRP could be as low as 10, and a later study of bone tumors in dogs reviewed by the NRPB (1993) gave values in the range of 4-6. An earlier evaluation of lung tumors in animals by the ICRP (1980) suggested values in the range of 6-40 with an average of about 30. A more recent review by the NRPB (1993) considered data on transformation and mutation of mammalian cells as well as induction of tumors and chromosome aberrations in animals. If the study that used *X* rays as the reference radiation is excluded, estimates of RBE obtained from the different studies are in the range of 4-40, and the average is about 22. All estimates described above represent values at low, protracted doses; i.e., they are values of RBE_M.

Based on the distribution of values of RBE_M for all biological effects included in the review by the NRPB (1993), we propose that the radiation weighting factor for alpha particles at low doses and dose rates, $w_{R,L}$, be described by a triangular probability distribution having a

lower bound of 3, a mode of 24, and an upper bound of 45; the arithmetic mean of this distribution is equal to the mode. This probability distribution also provides a reasonable representation of the data on RBE_M for animal tumors only. The proposed probability distribution is triangular, rather than lognormal as in the case of neutrons, because the distribution of values of RBE_M appears to be more symmetrical about the arithmetic mean. The bounds of the triangular distribution encompass the highest and lowest reported values, taking into account the uncertainties in the extreme values. Since the distribution has a specified lower bound greater than 1.0, truncation of the lower tail at 1.0, based on an assumption that the biological effectiveness of alpha particles would not be less than that of high-energy photons, is not needed. The proposed probability distribution of $w_{R,L}$ would be used to estimate cancer risks in humans at low doses and dose rates of alpha particles using eq. (2). Acute exposure to alpha particles emitted by radionuclides generally should not be of concern.

As in the case of neutrons, an additional consideration in estimating cancer risks from exposure to alpha particles at low doses and dose rates is the possibility of an inverse dose-rate effect, whereby the biological effectiveness at a given dose increases as the dose rate decreases. An analysis of data in humans (underground miners) who were exposed to elevated levels of radon has shown an inverse dose-rate effect that could be as much as a factor of 3 but is more likely less than a factor 2 (Lubin et al., 1995). For the following reasons, however, we do not recommend that the proposed radiation weighting factor, $w_{R,L}$, for alpha particles at low doses and dose rates be adjusted to account for a possible inverse dose-rate effect. First, the effect is not observed in underground miners at exposures to radon decay products below 50 Working Level Months (WLM) (Lubin et al., 1995), and the observed effects at higher exposures may be due, at least in part, to cell killing at the highest dose rates. Second, in contrast to neutron studies in animals, studies using alpha-emitting radionuclides involved protracted exposures, and the estimated RBEs may already include any inverse dose-rate effect. Finally, again in contrast to neutrons, the RBEs for alpha particles are extrapolated values at low doses and dose rates, RBE_M, and the highest values, which correspond to the highest DDREFs for the reference low-LET radiations, may be conservative when applied to humans. We also note that the inverse dose-rate effect for alpha particles in humans, if it is real, is likely to be quite small compared with the uncertainty in the radiation weighting factor, $w_{R,L}$.

Radiation Weighting Factors for Electrons

With the exception of very low-energy electrons emitted in beta decay of ^3H, we are not aware of any studies that directly investigated the biological effectiveness of electrons relative to photons. Therefore, we propose that the radiation weighting factor for all electrons except those emitted in ^3H decay (or electrons of comparably low energies) be set to 1.0, without uncertainty, as is the customary practice in radiation protection (ICRP, 1991; NCRP, 1993).

Beta radiations from ^3H decay are known to be biologically more effective than gamma rays in inducing stochastic effects (NCRP, 1990; Straume and Carsten, 1993). Based on a

previous analysis by *SENES* Oak Ridge (Thomas and Hoffman, 2000), we recommend a triangular probability distribution of the radiation weighting factor, $w_{R,L}$, for ^3H having a lower bound of 1.0, a mode of 2.0, and an upper bound of 5.0. The arithmetic mean of this distribution is 2.6. The recommended probability distribution of $w_{R,L}$ would be used to estimate cancer risks in humans in accordance with eq. (2). Acute exposures to ^3H generally should not be of concern.

The recommended probability distribution of $w_{R,L}$ for ^3H described above is about the same as the recommended distribution of $w_{R,L}$ for *X* rays discussed previously. This comparison is consistent with data which show that ^3H and *X* rays are about equally effective in inducing stochastic effects (NCRP, 1990). The recommended $w_{R,L}$ for ^3H also would be used when the dose is due primarily to other electrons of comparably low energies.

Summary of Recommended Radiation Weighting Factors

Based on evaluations of data on the biological effectiveness of various ionizing radiations, we have developed recommendations on radiation weighting factors for use in estimating the probability of causation of cancers in humans based on cancer risks at high doses and high dose rates of high-energy gamma rays obtained from studies in the Japanese atomic-bomb survivors. These recommendations are summarized as follows.

- For neutrons, cancer risks in humans at any dose and dose rate should be estimated using eq. (3). For fission neutrons, the proposed probability distribution of the radiation weighting factor at high doses and high dose rates of the reference gamma radiation, $w_{R,H}$, is lognormal with an arithmetic mean of 6 and an upper 97.5% confidence limit of 20; the 95% confidence interval of this distribution lies between 1.2 and 20. When the neutron energy is outside the range of 0.1-2 MeV, the probability distribution of $w_{R,H}$ should be obtained by scaling (reduction) of the probability distribution for fission neutrons by a factor which is based on the step function for the radiation weighting factor for neutrons recommended by the ICRP (1991). At energies of 10-100 keV or 2-20 MeV, we propose that the scaling factor that is applied to the probability distribution of $w_{R,H}$ for fission neutrons be described by a triangular probability distribution having a minimum of 1.5, a mode of 2, and a maximum of 4; and at energies of <10 keV or >20 MeV, the scaling factor should be described by a triangular probability distribution having a minimum of 3, a mode of 4, and a maximum of 6. In addition, under conditions of chronic exposure only, an enhancement factor representing the inverse dose-rate effect for high-LET radiations should be applied to the radiation weighting factor for neutrons of any energy. We propose that the enhancement factor for chronic exposure to neutrons be described by a discrete probability distribution having 50% of the values at 1, 25% at 1.5, and 25% at 2. After all relevant adjustments for the exposure situation of concern are applied to the radiation weighting factor for fission neutrons, $w_{R,H}$, the lower tail of the resulting probability distribution should be truncated at 1.0, based on an assumption that the biological effectiveness of neutrons should not be less than that of high-energy photons.

- For photons of energy less than 200 keV, cancer risks in humans at low doses and dose rates should be estimated using eq. (2), and the radiation weighting factor, $w_{R,L}$, should be described by a lognormal probability distribution having a 95% confidence interval between 1.9 and 3.7. This distribution is equivalent to an estimated $w_{R,L}$ of 2.6 ± 0.5, where the uncertainty is the standard deviation. In estimating cancer risks at incident photon energies less than 30 keV, the probability distribution of $w_{R,L}$ should be increased by a factor described by a triangular probability distribution having a minimum of 1.0, a mode of 1.3, and a maximum of 1.6. Under conditions of acute exposure, cancer risks in humans also would be estimated using eq. (2), except the probability distribution or single value of $DDREF_\gamma$ would not be the same as the probability distribution of $DDREF_\gamma$ that is assumed in cases of chronic exposure.

- For alpha particles of any energy emitted by radionuclides, cancer risks in humans at low doses and dose rates should be estimated using eq. (2), and the radiation weighting factor, $w_{R,L}$, should described by a triangular probability distribution having a minimum of 3, a mode and arithmetic mean of 24, and a maximum of 45. We do not recommend any adjustment to account for the possibility of a small inverse dose-rate effect. Acute exposures to alpha particles emitted by radionuclides should not be of concern.

- For electrons, cancer risks in humans should be estimated using eq. (2), and a radiation weighting factor, $w_{R,L}$, other than 1.0 should be used only in the case of internal exposure to beta radiation emitted in ^3H decay or in other situations where the electron energies are comparably low. We propose that the radiation weighting factor for ^3H be described by a triangular probability distribution having a minimum of 1.0, a mode of 2.0, and a maximum of 5.0.

The recommendations developed in this report also are summarized in Table 1. In this table, the aggregate factors that would be used to modify estimated cancer risks from exposure to high-energy photons, either at low doses and dose rates or at high doses and high dose rates, for the purpose of estimating cancer risks in humans are referred to as RBE factors, to be consistent with the nomenclature used in the IREP code.[3] When more than one factor contributes to the RBE factor for a particular radiation type, the probability distribution of the RBE factor is the aggregate distribution that is obtained by combining the recommended probability distributions of the individual factors. For example, the probability distribution of the RBE factor for chronic exposure to neutrons of energy 10-100 keV is the result of combining the separate probability

[3]Although the term "RBE factor" is used to describe the assumed biological effectiveness of different radiations in inducing cancers in humans, these factors are not really RBEs. Strictly speaking, the term RBE applies only to the results of specific radiobiological experiments, but the RBE factors in humans generally are assumed values that are based on evaluations of a variety of studies in other biological systems.

distributions of the radiation weighting factor for fission neutrons, $w_{R,H}(n)$, the reduction factor to account for the biological effectiveness of 10-100 keV neutrons compared with fission neutrons, denoted by AF_2, and the correction for the inverse dose-rate effect, denoted by EF.

In estimating cancer risks from exposure to neutrons, we assume that the RBE factor cannot be less than 1.0, based on the consideration that the biological effectiveness of neutrons should not be less than that of high-energy photons. This truncation is performed in the IREP code after the full, untruncated probability distribution of the relevant RBE factor is obtained.

Table 1. Summary of relative biological effectiveness (RBE) factors to be used in estimating probability of causation of cancers from exposure to various radiation types. For description of radiation weighting factors (w) and other terms, see Legend on following page.

Exposure information			Estimated RBE factor		
			95% confidence interval		
Radiation type	**Exposure rate**	**Description**	**2.5th**	**50th**	**97.5th**
RBE factors to be used with risk coefficients derived from exposures at high doses and high dose rates of gamma radiation and adjusted to low doses and dose rates by use of $DDREF_\gamma$					
Electrons	Any[a]				
All except tritium		Single-valued	—	1.0	—
Tritium		Triangular (1, 2, 5)	1.3	2.6	4.4
Photons	Any[a]				
E>200 keV		Single-valued	—	1.0	—
E=30-200 keV		$w_{R,L}(X)$	1.9	2.7	3.7
E<30 keV		$w_{R,L}(X)$ × Triangular (1, 1.3, 1.6)	2.4	3.4	5.0
Neutrons		Not applicable			
Alpha particles	Chronic[b]	$w_{R,L}(\alpha)$	7.7	24	40
RBE factors to be used with risk coefficients derived from exposure to high doses and high dose rates of gamma radiation					
Electrons		Not applicable			
Photons		Not applicable			
Neutrons[c]					
E=0.1-2 MeV[d]	Acute	$w_{R,H}(n)$	1.2	4.9	20
	Chronic	$w_{R,H}(n)$ × EF	1.3	6.4	30
E=10-100 keV or	Acute	$w_{R,H}(n)/AF_2$	1.0	2.3	9.4
E=2-20 MeV	Chronic	$w_{R,H}(n)$ × EF/AF_2	1.0	3.0	13
E<10 keV or	Acute	$w_{R,H}(n)/AF_4$	1.0	1.1	4.6
E>20 MeV	Chronic	$w_{R,H}(n)$ × EF/AF_4	1.0	1.5	7.2
Alpha particles		Not applicable			

See following page for footnotes.

Footnotes for Table 1

[a]For acute exposures to photons or electrons, risk coefficients are adjusted by a $DDREF_\gamma$ that depends on the dose received. For acute doses greater than 20 cSv, $DDREF_\gamma = 1.0$. For acute doses less than 20 cSv, a $DDREF_\gamma$ different from unity is applied, and its value approaches $DDREF_\gamma$ for chronic exposures as the dose approaches zero.

[b]Exposures to alpha particles emitted by radionuclides generally should be chronic.

[c]The lower tail of the aggregate probability distribution for each exposure situation is truncated at 1.0, based on an assumption that the biological effectiveness of neutrons should not be greater than that of high-energy photons.

[d]The RBE factors for this energy range apply to fission neutrons.

Legend for Table 1

RBE factor	Relative biological effectiveness factor obtained by combining radiation weighting factor for a given radiation type with any applicable modifying factors.
$w_{R,L}(X)$	Radiation weighting factor for *X* rays and gamma rays of energy <200 keV. Probability distribution assumed to be lognormal (GM=2.65; GSD=1.19).
$w_{R,H}(n)$	Radiation weighting factor for fission neutrons derived from experiments using high acute doses of high-energy gamma radiation. Probability distribution assumed to be lognormal (GM=4.89; GSD=2.05).
EF	Enhancement factor to account for inverse dose-rate effect; applies only to chronic exposures to neutrons of any energy. Probability distribution assumed to be discrete (50% at 1.0, 25% at 1.5, 25% at 2).
AF_2	Energy-dependent reduction in biological effectiveness, relative to fission neutrons, for neutrons of energy 10-100 keV or 2-20 MeV. Probability distribution assumed to be triangular (min=1.5, mode=2, max=3).
AF_4	Energy-dependent reduction in biological effectiveness, relative to fission neutrons, for neutrons of energy <10 keV or >20 MeV. Probability distribution assumed to be triangular (min=3, mode=4, max=6).
$w_{R,L}(\alpha)$	Radiation weighting factor for alpha particles derived from experiments using low dose rates of low-LET reference radiations. Probability distribution assumed to be triangular (min=3, mode=24, max=45).
$DDREF_\gamma$	Dose and Dose-Rate Effectiveness Factor used to adjust risk coefficients derived from exposures at high doses and high dose rates of high-energy gamma radiation in cases of exposure at low doses and dose rates of low-LET radiations.

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